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## STATEMENT

**Assoc. Prof. Mihael Emilov Tsalta-Mladenov, MD, PhD**

Associate professor at the department of Neurology and Neuroscience, Faculty of Medicine,  
Medical University “Prof. Dr. Paraskev Stoyanov”- Varna.

**Member of the Scientific Jury, appointed by Order No. P-109-476/20.11.2025 of the Rector  
of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.**

Regarding the Dissertation Thesis

**of Paola Nikolay Kulicheva, MD**

**on the topic: „Predictive Factors for Mortality in Young and Middle-Aged Patients with  
Ischemic Stroke“**

**for the awarding the educational and scientific degree „Doctor“ in the field of higher**

**education 7. Health and Sports, professional direction 7.1. Medicine, and**

**the doctoral program „Neurology“**

**Scientific Supervisor: Assoc. Prof. Darina Kirilova Georgieva-Hristova, MD, PhD**

Based on Order No. P-109-476/20.11.2025 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, and in accordance with the decision of the Scientific Jury based on Protocol No. 1/02.12.2025, I have been assigned to prepare a statement (in Bulgarian and English) on the dissertation thesis entitled "Predictive factors for mortality in young and middle-aged patients with ischemic stroke"

The statement has been prepared in accordance with the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria and the Regulations for the Development of Academic Staff of Medical University "Prof. Dr. Paraskev Stoyanov"-Varna.

All stages of the doctoral thesis preparation have been fully completed. A change in the topic of the dissertation thesis has been approved in accordance with Order No. R-109-211/27.03.2023 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna, from "Follow-up of survival in patients with epileptic seizures after stroke" to "Predictive factors for mortality in young and middle-aged patients with ischemic stroke". There has been no change in the scientific supervisor. The candidate has submitted all required documents and materials in compliance with the procedural requirements for obtaining the academic degree of 'Doctor,' as stipulated by the regulations of the Medical University 'Prof. Dr. Paraskev Stoyanov' - Varna.

#### **I. Brief Biographical and Professional Data of the Candidate:**

Dr. Paola Nikolay Kulicheva obtained her educational and qualification degree "Master" in Medicine at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna in 2017. In 2023, she acquired a specialty in Neurology.

Dr. Paola Nikolay Kulicheva began her professional career in October 2017 at the Center for Emergency Medical Care – Varna. Since April 2018, she has been working as a physician in the Emergency Pediatric Unit at MBAL "St. Anna" – Varna. From September 2018 to the present, she has been employed as a physician in the Intensive Care Unit for Neurological Diseases at the Second Clinic of Neurology of the University Hospital "St. Marina" – Varna.

She participates annually in national and international scientific forums. In July 2023, she completed specialized training in ultrasound diagnostics of the nervous system (Neurosonology).

She is a member of professional and scientific organizations, including the Bulgarian Medical Association and the Bulgarian Society of Neurology.

#### **II. Relevance of the Topic:**

Ischemic stroke represents one of the leading causes of mortality and long-term disability on both a global and national scale. Over recent decades, a clear trend toward an increasing incidence of the disease has been observed among young and middle-aged patients- a population characterized by high social and economic activity. The consequences of stroke in this age group result not only in disability and mortality, but also in severe socio-economic burden.



The clinical course and prognosis of ischemic stroke in young and middle-aged patients are characterized by marked heterogeneity and often differ significantly from those observed in older individuals. This is attributable to specific etiological mechanisms, distinct risk profile, and a relatively higher prevalence of less commonly documented and non-traditional risk factors.

Despite the growing scientific interest in this topic, available data on independent predictors of mortality in young and middle-aged patients with ischemic stroke remain limited and frequently contradictory.

In Bulgaria, at the time of conducting the present scientific study, there has been no other research specifically aimed at a comprehensive investigation of various predictive factors for mortality in patients with ischemic stroke in young and middle-aged adults. The present dissertation addresses this problem in depth and offers a methodological analysis that contributes to the expansion of scientific knowledge in this field.

For all these reasons, the chosen dissertation topic is timely, innovative, and of exceptional significance for both scientific research and clinical practice.

### **III. Characteristics, Scope and Structure of the Dissertation thesis:**

The dissertation thesis of Dr. Paola Nikolay Kulicheva comprises 174 pages and includes 46 figures and 41 tables. It is written in Bulgarian and demonstrates an excellent command of highly specialized terminology. The dissertation is structured into the following main sections:

#### **1. Literature Review (42 pages):**

The literature review is very well structured, comprising a total of eight sections, in which multiple aspects of the specified topic are examined, including the etiological classification of ischemic stroke, risk factors—modifiable and non-modifiable, less frequently documented risk factors characteristic of young and middle-aged patients, assessment scales—clinical and radiological, as well as an in-depth review of clinical, laboratory, and neuroimaging prognostic markers for fatal outcome. The main emphasis of the literature review is placed on risk factors and their predictive value for mortality in patients with ischemic stroke in young and middle-aged adults.

The doctoral candidate has used contemporary international and national scientific sources and demonstrates excellent theoretical training and profound knowledge of the research topic.

#### **2. Aim, Objectives, and Working Hypotheses (1 page)**

The in-depth and analytical review of the contemporary scientific literature, as well as the excellent familiarity with the investigated problem, form the basis for the clear and accurate formulation of the scientific aim of the dissertation thesis, namely, to identify and analyze the clinical, laboratory, and neuroimaging predictive factors for mortality in patients with ischemic stroke in young and middle-aged adults.

In order to achieve this aim, eight specific scientific objectives have been formulated. These objectives are logically justified, mutually complementary, and fully consistent with the



aim of the study. They are clearly and logically defined on the basis of the available literature data and the results of previous studies.

### **3. Material and methods (4 pages)**

To achieve the aim and objectives of the present dissertation thesis, a clinical, observational, retrospective study was conducted among patients with acute ischemic stroke in young and middle-aged adults.

The study included a total of 168 patients, divided into two main groups: a target group comprising 67 patients aged 18 to 59 years with a fatal outcome during hospitalization, and a control group of 101 patients in the same age range who survived an ischemic stroke.

The inclusion and exclusion criteria for study participants, as well as the methods used to accomplish the defined objectives and scientific aim, are clearly and unambiguously presented by the doctoral candidate.

Established clinical and assessment scales were applied in the study to evaluate stroke severity and level of consciousness, along with imaging and laboratory parameters with proven prognostic value.

The work on the dissertation thesis was carried out in full accordance with the principles of good scientific practice, following approval by the Research Ethics Committee at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna (Decision No. 133/22.06.2023).

The described statistical methods were appropriately selected and aligned with the aims and design of the study. These include descriptive statistical methods, graphical methods for result visualization, univariate analytical approaches to assess associations between individual variables and fatal outcome, as well as multivariate logistic regression analysis for the identification of independent predictors of mortality. The development and application of predictive statistical models further enhance the informative value and clinical applicability of the obtained results.

The selected and applied statistical methods allow for reliable processing of the collected data.

### **4. Original Results (59 pages)**

In this section, Dr. Paola Nikolay Kulicheva presents the results of the conducted study in a detailed and systematic manner, demonstrating the complete and successful fulfillment of all defined objectives directly related to the main aim of the dissertation thesis. The presented results are fully sufficient in both scope and content and allow for the well-founded formulation of conclusions regarding predictive factors for mortality in patients with ischemic stroke in young and middle-aged adults.

The results are logically and consistently systematized and are illustrated by a large number of tables and figures, accompanied by clear descriptions. The selection of visualizations is appropriate and corresponds to the correctly applied statistical methods used for the analysis of the collected data.

The results are structured and distributed into six subsections:

- Characteristics of the studied population;
- Analysis of non-modifiable and modifiable risk factors and their association with fatal outcome;

- Assessment of the severity of neurological deficit (NIHSS) and level of consciousness (GCS) and their association with fatal outcome;
- Analysis of other clinical parameters, neuroimaging findings, and laboratory markers as potential prognostic factors;
- Evaluation of etiological subtypes of ischemic stroke according to the TOAST classification;
- Univariate and multivariate logistic regression analysis, on the basis of which predictive models were developed.

## **5. Discussion (26 pages)**

In this section of the dissertation thesis, Dr. Paola Nikolay Kulicheva once again demonstrates excellent knowledge of the international scientific literature on the investigated problem. The obtained results are interpreted in a critical and well-argued manner and are compared with data from large international studies, meta-analyses, as well as data from various national registries.

The discussion comprehensively addresses the role of non-modifiable and modifiable risk factors, clinical status at admission, imaging and laboratory parameters, as well as the etiological subtypes of ischemic stroke in determining prognosis in young and middle-aged patients. Particularly valuable is the analysis of less frequently documented risk factors and their role within the prognostic model.

The section is presented in a logical structure, a sound and critical comparison between the author's own results and the existing scientific data, and an emphasis on the clinical significance of early prognostic assessment and the opportunities for optimizing therapeutic strategies.

## **6. Conclusions and Contributions (3 pages)**

The dissertation thesis concludes with the formulation of six specific conclusions derived from the conducted research, as well as four scientific contributions, which logically follow from the presented results.

The scientific contributions are clearly delineated and may be summarized as contributions of an original nature, related to the development and validation of multifactorial predictive models, as well as contributions of scientific and applied significance, aimed at improving early prognostic assessment and clinical decision-making in this specific patient population.

## **7. References (22 pages)**

The bibliographic reference list includes 253 literature sources—6 in Cyrillic and 247 in Latin script, with 168 sources (66%) published within the last 10 years.

## **8. Publications and Scientific Activities Related to the Dissertation (1 page)**

Dr. Paola Nikolay Kulicheva has presented a list of two full-text publications related to the dissertation thesis—one published in a Bulgarian scientific journal, in which she is the first author, and a second published in an international peer-reviewed journal, in which she is the second author.



The full-text articles published in connection with the dissertation thesis fully comply with the regulatory requirements for doctoral candidates' publication activity for the awarding of the educational and scientific degree "Doctor," as stipulated in the Law for the Development of Academic Staff in the Republic of Bulgaria and the internal regulations of the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

#### **9. Dissertation Thesis Summary**

The dissertation thesis summary is prepared in Bulgarian and English and comprises a total of 63 pages, including 31 figures and 26 tables. It is structured in accordance with the established requirements, and its content fully corresponds to the dissertation thesis.

#### **IV. Critical Remarks**

I have no critical remarks to report.

#### **V. Conclusion**

The dissertation thesis submitted for review is an original work by the author, characterized by originality, relevance, depth of analysis, demonstration of substantial scientific knowledge, and significant scientific and applied value.

Dr. Paola Nikolay Kulicheva is an excellent neurologist, demonstrating a high level of professional commitment and responsibility in her work with patients suffering from a wide spectrum of neurological disorders, including conditions requiring neurointensive care. In the course of her research activity, she has invested considerable effort, patience, perseverance, and personal dedication, which has enabled her to successfully combine intensive clinical practice with the development and completion of a thorough and scientifically valuable dissertation thesis.

For all the reasons stated above, I confidently give my positive assessment of the presented dissertation thesis and propose to the members of the esteemed Scientific Jury to vote positively and award the educational and scientific degree "Doctor" to Paola Nikolay Kulicheva MD in the doctoral programme in the scientific specialty "Neurology."

09.01.2026

Prepared the statement:

Заличено на основание чл. 5,  
§1, б. „В“ от Регламент (ЕС)  
2016/679

Varna

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